Comparative study of two agents in axillary brachial plexus block: Bupivacaine vs Levobupivacaine

Karağaç brakial pleksus bloğunda iki ajana karşılaştırılan çalışma: Bupivakain ve Levobupivakain

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Abstract

Objective: The prospective, randomized study aimed to investigate whether there is significant difference between the block and analgesic quality variables of morphine adjuncted bupivacaine and levobupivacaine in axillary perivascular brachial plexus.

Material and Methods: Thirty five ASA physical status I-II patients, aged 18-70 years scheduled for upper limb surgery under axillary brachial plexus anaesthesia were randomly allocated into two groups. Group B (n:20): 40 mL 0.375% bupivacaine + 2 mg morphine and Group L (n:15): 40 mL 0.375% levobupivacaine + 2 mg morphine. Sensorial block onset time, motor block onset time, duration of sensorial block and first analgesic requirement time were recorded in each of the groups.

Results: Significant difference between axillary levobupivacaine and bupivacaine performed groups respect to sensorial block onset time (Group B: 13.40±2.76 minutes, Group L: 9.66±2.52 minutes, p<0.0001), motor block onset time (Group B: 9.20±1.73 minutes, Group L: 6.40±2.55 minutes, p<0.0001) and duration of sensorial block (Group B: 1167.15±48.14 minutes, Group L: 1057.33±48.14 minutes, p<0.0001) were found.

Conclusion: We think that levobupivacaine may be preferred for its rapid sensorial and motor onset time.

Key words: axillary brachial plexus block, levobupivacaine, bupivacaine.

Özet

Amaç: Bu prospektif randomize çalışmada; aksiller perivasküler brakial pleksusda, morfin destekli bupivakain ve levobupivakainin blok ve analjezik kalite açısından belirgin farklılık gösterip göstermediğinin araştırılması amaçlanmıştır.

Gereç ve Yöntem: Brakial pleksus anestezisi altında üst ekstremite cerrahisi planlanan, 18-70 yaş arası, ASA fiziksel durumu I-II olan 35 hasta rastgele iki gruba ayrıldı. Grup B (n:20): 40 mL %0,375 bupivakain + 2 mg morfin ve grup L (n:15): 40 mL %0,375 levobupivakain + 2 mg morfin. Duyusal blok başlangıç zamanı, motor blok başlangıç zamanı, duyusal blok süresi ve ilk analjezik gereksinim süresi grupların her birinde kaydedildi.

Bulgular: Uygulanan gruplarda, aksiler levobupivakain ve bupivakain arasinda duyusal blok başlangıç zamanı açısından (Grup B: 13.40±2.76 dakika, Grup L: 9.66±2.52 dakika, p<0.0001), motor blok başlangıç zamanı açısından (Grup B: 9.20±1.73 dakika, Grup L: 6.40±2.55 dakika, p<0.0001), ve duyusal blok süresi açısından (Grup B: 1167.15±48.14 dakika, Group L: 1057.33±48.14 dakika, p<0.0001) anlamlı ilişki tespit edildi.

Sonuç: Hızlı duyusal ve motor başlangıç zamanlarından dolayı, levobupivakainin tercih edilebileceğini düşünmektediyiz.

Anahtar kelimeler: aksiler brakial pleksus bloğu, levobupivakain, bupivakain

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Introduction

For over a century, brachial plexus anesthesia has been an indispensable tool in the anesthesiologist’s armamentarium (1). Axillary block of the brachial plexus is a common, simple and safe anaesthetic technique for distal upper extremity surgery; often for elbow, forearm and hand surgery. Different techniques can be used to achieve block on using perivascular approach to brachial plexus (1,2,3).

Levobupivacaine is a long acting local anaesthetic with a clinical profile closely resembling that of bupivacaine (4). It is a relatively new long-acting local anesthetic that have been developed after reports of simultaneous seizure and cardiac arrest with prolonged resuscitation after accidental intravascular injection of bupivacaine (5). The use of levobupivacaine is described for peripheral nerve blocks besides epidural, caudal, and spinal anesthesia and the agent is used for all common indications in a wide range of clinical settings (6,7).

Regional anesthesia is becoming increasingly popular for orthopaedic surgery as it offers several advantages over general anesthesia and a trend towards more peripheral and selective nerve blocks exists (8). By this aim; for upper limb surgery; interscalene blocks are ideally suited for shoulder and upper arm surgery, supraclavicular nerve blocks for upper arm, elbow and radial side of forearm, and the infraclavicular and axillary block are suited for hand, wrist and forearm surgery. (2). Since then; axillary block of the brachial plexus is a suitable anaesthetic technique both for orthopaedic, plastic and peripheral vascular surgery procedures performed distal to the elbow. Also; in emergency surgery, axillary brachial plexus blocks represent more than 50% of all regional anesthesia techniques performed with midhumeral brachial plexus block (9).

This study aimed to investigate whether there is a significant difference between the block and analgesic quality variables of morphine adjuncted bupivacaine and levobupivacaine in axillary perivascular brachial plexus.

Methods

Study protocol of this prospective, controlled, single-centre trial had been approved by the local Ethics Committee. Before entering the study, written informed consent was obtained from 35 ASA physical status I-II patients, aged 18-70 years, scheduled for surgery in the upper extremities. Patients who could not cooperate, were pregnant or were allergic to amide local anesthetics, patients taking medications with psychotropic or adrenergic activities and patients receiving chronic analgesic therapy other than simple analgesics (e.g. non-steroidal anti-inflammatory drugs) were barred from the study.

After establishing an IV line by an 18-gauge catheter in a peripheral vein in the contra-lateral arm; 0.05 mg.kg⁻¹ intravenous (IV) midazolam was given as premedication 10 minutes before block placement. Standard monitoring was used throughout the study, including arterial blood pressure, heart rate and pulse oximetry. The surgical procedure was always performed using a standard tourniquet inflated 100 mmHg higher than systolic arterial blood pressure. Hemodynamic variables were measured and recorded before block placement (baseline values), 1 and 5 minutes after block placement and 5 minute intervals until the end of surgery.

Anaesthetic solution was prepared according to a random number table by an anaesthesit not involved in the study. Also the block performing and results observing anaesthetists were blinded to the treatment group. Using a sealed envelope technique, patients were allocated into two groups: Group B (n: 20): 40 mL 0.375% bupivacaine + 2 mg morphine and Group L (n: 15): 40 mL 0.375% levobupivacaine + 2 mg morphine.

In each of the groups; the nerve block was performed with the patient lying supine, arm abucted to about 90°, and the hand resting on a pillow next to the head. The axillary pulse was identified and the injection area was disinfected. For local anesthesia; injection site was infiltrated with 1 mL of lidocaine 2% subcutaneously. A 0.71 × 80 mm, 22 G needle (Stimuplex D®, B. Braun Melsungen, Germany) was connected to a nerve stimulator (Stimuplex® HNS 12, B. Braun Melsungen AG Germany) and inserted above the axillary artery. A motor response in the hand was first sought by stimulating with 1 mA. If a peripheral motor response corresponding to the median, radial or ulnar nerve stimulating response was accepted. Stimulation frequency was set at 2 Hz, while the intensity of stimulating current was initially set to deliver 1 mA and then gradually decreased to ≤0.5 mA after each muscular twitch was observed. A multiple injection technique was used eliciting specific twitches on nerve stimulation to confirm exact needle location.

Nerves were located as follows: musculo-cutaneous by arm flexion; radial by arm and/or wrist and finger extension; median by flexion of the wrist and 2nd and 3rd fingers; ulnar by flexion of the 4th and 5th fingers and adduction of the thumb. If the injection of 1 mL of the study solution immediately stopped the muscular contraction, the needle location was considered adequate and the remaining volume of local anaesthetic solution
was injected. A volume of 10 mL was injected at each nerve twitch, for a total volume of 40 mL. During injection, negative aspiration was performed every 5-7 mL to avoid intravascular injection. Immediately after injection has been stopped; the arm was kept adducted and the hand resting on the chest.

Sensory and motor blocks on the operation planned arm were evaluated with 5 minutes intervals after the injection has been stopped until the surgical anaesthesia was achieved.

Sensory block in the surgical procedure planned site was tested with a 22-gauge hypodermic needle by using the pinprick test and compared with the same stimulation in the contra lateral hand.

- (1) 0 (no block): normal sensitivity
- (2) 1 (onset): reduced sensitivity compared with the same territory in the contralateral upper limb
- (3) 2 (partial): analgesia or loss of the sharp sensation of the pinprick
- (4) 3 (complete): anesthesia or loss of sensation to touch

Motor block was assessed by thumb opposition for the median nerve, thumb abduction for the radial nerve, and flexion of the elbow for the musculocutaneous nerve.

- (1) 0: no block
- (2) 1 (onset): decreased movement with loss of strength
- (3) 2 (partial): decreased movement with inability to perform movement against resistance
- (4) 3 (complete): paralysis

Sensory and motor blocks were assessed in each nerve territory at 2, 5, 10, 15, 20, 25, and 30 mins after LA injection. Patients were considered to be ready for surgery when scores were 2 (partial sensory and motor block).

As soon as sensorial and motor blocks were evaluated below variables were recorded:

**Time to Onset of Sensory Block (minute):** Time between the end of last injection and the total abolition of the pinprick response, and complete paralysis in all of the nerve distributions respectively.

**Time to Onset of Motor Block (minute):** time to reach scores of 1 in each nerve.

**Duration of sensorial block (minute):** Time interval between withdrawal of the needle and reappearance of paresthesia in the 4 nerve distribution areas.

First analgesic requirement time (minute): Time interval between block placement and patients' first analgesic request.

In all instances, surgery was initiated 45 mins after LA injection. All patients had a tourniquet placed on the affected arm.

At the skin incision or during the procedure; 1 microgram/kg fentanyl intravenously was added when the patient has reported pain at the surgical site defined with Verbal Rating Scale Score ≥2 (Verbal Rating Scale Score; 0: No Pain, 1: Mild Pain, 2: Moderate Pain, 3: Severe Pain, 4: Unbearable Pain). If fentanyl supplementation did not provide adequate analgesia, 1 mg/kg propofol bolus was to be given and followed by a continuous IV infusion (2-4 mg/kg/h). According to the need for supplementary intravenous analgesia, the quality of nerve block was evaluated as follows:

- Satisfactory nerve block= No analgesia required to complete surgery
- Unsatisfactory nerve block= Fentanyl supplementation required to complete surgery
- Failed nerve block= Fentanyl and propofol administration required to complete surgery.

Mean arterial blood pressure (MAP) and heart rate (HR) were recorded before application of the block as well as immediately 1 and 5 minutes after block and 5 minute intervals until 30 minute and with 30 minute intervals thereafter, until the end of the operation. Peripheral oxygen saturation was monitored by pulse oximeter device and observed continously but was not recorded among the study data since all of the patients were given 2 L/min O₂ by nasal cannula and oxygen saturation was between 97% and 100% in all of the patients.

Sensory and motor blocks were assessed at 6, 12, 18, and 24 hrs after LA injection, even during nighttime. Sensory block was evaluated in the territory of the median nerve, by pinprick with a 22-gauge needle.

For the duration of the study the presence of hypotension (30% decrease over baseline values), presence of bradycardia (heart rate, <50 beats/min), hypoxia (O₂ saturation, <=90%), or nausea and vomiting was recorded and treated according to standard clinical practice.

The statistical analysis of sex, comorbidities, ASA physical status, type of surgery between groups were performed with Mann-Whitney-U and Two-Sample Kolmogorov-Smirnov Test. Analysis of age, operation time, sensorial and motor block onset time between groups were done using Independent Samples-t Test. The statistical significance of variations of hemodynamical parameters HR and MAP between control values and measurement periods were calculated with Paired Samples-t Test. Data are expressed as mean values (SD). p < 0.05 considered statistically significant.
Results

Total 40 patients were included in the study, five of them excluded. All performed blocks were adequate for the proposed surgery and the quality of nerve block was defined satisfactory nerve block for all of all the patients. Analysis of patient characteristics demonstrated no significant differences between groups according to age (p:0.166), comorbidity (p:0.114), ASA physical status (p:0.207), total operation time (p:0.257) and gender (p:0.052). Demographic variables of each group are shown in Table 1.

Table 1. Mean age and operation time, sex, and presence of comorbidity of two groups (mean±SD)

<table>
<thead>
<tr>
<th></th>
<th>Group L (n=15)</th>
<th>Group B (n=20)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year±SD)</td>
<td>47.13±19.71</td>
<td>37.70±19.36</td>
<td>0.166</td>
</tr>
<tr>
<td>Comorbidity</td>
<td>8</td>
<td>5</td>
<td>0.114</td>
</tr>
<tr>
<td>ASA (I/II/III)</td>
<td>8/6/1</td>
<td>15/3/1</td>
<td>0.207</td>
</tr>
<tr>
<td>Operation time (minute±SD)</td>
<td>98.60±64.61</td>
<td>125.90±72.47</td>
<td>0.257</td>
</tr>
<tr>
<td>Sex (F/M)</td>
<td>2/13</td>
<td>7/13</td>
<td>0.052</td>
</tr>
</tbody>
</table>

Type of surgery in each of the groups were presented in Table 2.

Table 2. Type of surgery performed

<table>
<thead>
<tr>
<th></th>
<th>Group L</th>
<th>Group B</th>
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</thead>
<tbody>
<tr>
<td>Minor surgery of forearm trauma</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>Dupuytren’s contracture</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>A-V fistula repair</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Crush injury of arm and forearm</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Fracture of digits</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

Mean arterial pressure and heart rate showed no significant inter-group differences between control values and each of the study periods intervals both in Group B and Group L. Hemodynamic alterations within each group during study periods were shown in Table 3 and 4.

Table 3. Hemodynamic alterations in Group L (mean±SD)

<table>
<thead>
<tr>
<th></th>
<th>MAP</th>
<th>HR</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>103.67±18.06</td>
<td>77.80±12.63</td>
<td>-</td>
</tr>
<tr>
<td>Post-Block 1st min</td>
<td>102.00±19.24</td>
<td>79.27±11.91</td>
<td>0.344</td>
</tr>
<tr>
<td>Post-Block 5th min</td>
<td>99.33±19.33</td>
<td>77.20±12.37</td>
<td>0.773</td>
</tr>
<tr>
<td>Post-Block 10th min</td>
<td>101.40±18.94</td>
<td>75.87±12.64</td>
<td>0.392</td>
</tr>
<tr>
<td>Post-Block 15th min</td>
<td>101.33±18.95</td>
<td>75.07±12.57</td>
<td>0.133</td>
</tr>
<tr>
<td>Post-Block 30th min</td>
<td>105.80±21.60</td>
<td>74.27±12.50</td>
<td>0.056</td>
</tr>
<tr>
<td>Post-Block 60th min</td>
<td>101.33±21.10</td>
<td>71.93±11.94</td>
<td>0.002</td>
</tr>
<tr>
<td>Post-Block 90th min</td>
<td>103.60±20.25</td>
<td>71.13±12.04</td>
<td>0.003</td>
</tr>
<tr>
<td>Post-Block 120th min</td>
<td>10.00±19.73</td>
<td>70.73±10.55</td>
<td>0.003</td>
</tr>
</tbody>
</table>

P: Significance of MAP variations between control values and post-block periods,
P: Significance of HR variations between control values and post-block periods,
MAP values: mmHg±SD,
HR values: beat/minute (BPM)±SD.
Table 4. Hemodynamic alterations in Group B (mean±SD)

<table>
<thead>
<tr>
<th></th>
<th>MAP</th>
<th>p†</th>
<th>HR</th>
<th>P‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>88.40±15.05</td>
<td>-</td>
<td>83.00±10.24</td>
<td>-</td>
</tr>
<tr>
<td>Post-block 1st</td>
<td>88.05±12.21</td>
<td>0.887</td>
<td>78.40±11.13</td>
<td>0.003</td>
</tr>
<tr>
<td>Post-block 5th</td>
<td>86.00±14.13</td>
<td>0.302</td>
<td>80.40±10.88</td>
<td>0.090</td>
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<tr>
<td>Post-block 10th</td>
<td>88.40±14.43</td>
<td>1.000</td>
<td>78.40±9.46</td>
<td>0.009</td>
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<tr>
<td>Post-Block 15th</td>
<td>92.55±14.75</td>
<td>0.146</td>
<td>77.50±9.41</td>
<td>0.003</td>
</tr>
<tr>
<td>Post-Block 30th</td>
<td>96.60±13.38</td>
<td>0.024</td>
<td>78.00±9.33</td>
<td>0.004</td>
</tr>
<tr>
<td>Post-Block 60th</td>
<td>94.70±13.89</td>
<td>0.054</td>
<td>78.10±9.99</td>
<td>0.004</td>
</tr>
<tr>
<td>Post-Block 90th</td>
<td>98.55±18.36</td>
<td>0.020</td>
<td>79.00±9.78</td>
<td>0.031</td>
</tr>
<tr>
<td>Post-Block 120th</td>
<td>96.45±14.91</td>
<td>0.026</td>
<td>78.70±9.52</td>
<td>0.033</td>
</tr>
</tbody>
</table>

p† Significance of MAP variations between control values and post-block periods,
p‡ Significance of HR variations between control values and post-block periods,
MAP values: mmHg±SD,
HR values: beat/ per minute (BPM)±SD.

Time to Onset of Sensory Block was significantly different between groups (Group B: 13.40±2.76 minutes, Group L: 9.66±2.52 minutes, p <0.0001). Time to Onset of Motor Block was significantly different between groups (Group B: 9.20±1.73 minutes, Group L: 6.40±2.55 minutes, p<0.0001). Comparison of time to onset of sensory block and time to onset of motor block between two groups were demonstrated in Figure I.

Figure 1. Presentation of sensorial and motor block onset time differences in two groups (minutes)

Duration of sensorial block was significantly longer in Group B (1167.15±48.14 minutes) compared to Group L (1057.33±48.14 minutes, p<0.0001). Duration of sensorial block and first analgesic requirement time comparison between groups were demonstrated in Figure 2. First analgesic requirement time was not significantly different between groups (Group B: 1121.75±115.35 minutes, Group L: 1068.33±48.20 minutes, p:0.073).
Discussion

In the present study we found significant difference between axillary levobupivacaine and bupivacaine performed groups respect to sensory and motor block onset time and duration of sensorial block. First analgesic requirement time revealed no significant difference between groups.

Several studies have been performed to evaluate the efficiency of levobupivacaine and to compare the ability of this agent to achieve adequate analgesic and anaesthetic activity with the other local anaesthetics in peripheric blocks. D'Ambrosio et al (11) compared the onset time, anesthetic potency and adverse effects of three local anaesthetics (ropivacaine, levobupivacaine and bupivacaine) in both brachial and femoral plexus blocks and pointed out that duration of motor block and sensory block was respectively longer in levobupivacaine and bupivacaine administered groups equally. Cline et al (12) claimed that the first study has been performed by them measuring the differences in analgesic efficacy and latency when levobupivacaine and ropivacaine are used for brachial plexus anesthesia; and pointed out that duration of sensory analgesia was significantly longer with levobupivacaine and return of motor activity was significantly faster with ropivacaine and consequently concluded that levobupivacaine should be considered when postoperative analgesia is a concern but not when an early return of motor activity is required. A similar conclusion has been achieved in a study performed in orthopedic surgery of wrist and hand by Cacciaputi et al (13) and the duration of sensory block took longer time in a group of patients treated with levobupivacaine than racemic bupivacaine and ropivacaine. Our study’s results are in contradiction with those ones; since we have found shorter duration of sensory block with levobupivacaine than bupivacaine. This may be related to the concentration difference of the local anaesthetic solution prepared; in our study we have used 0.375% levobupivacaine although investigators have used 0.50% levobupivacaine in both two previous studies. The reason to prefer to use 0.375% solution of both bupivacaine and levobupivacaine in our study was the moderate operation times (approximately not longer than 2 hours) and morphine 2 mg adjucted to local anaesthetic solutions. As a conclusion of a study scheduled to assess differences in success rate of both large volume low concentration (40 mL 0.375%) and lower volume higher concentration (20 mL 0.75%) the investigators advised to administer local anaesthetics in larger volumes at lower concentrations to improve block quality (14). Zhao scheduled a study to investigate if low doses (36 mL) and low concentrations (0.1%) of levobupivacaine produce complete sensory blockade in preoperative axillary brachial plexus block compared to higher doses (72 mL) and concentrations (0.25%); and the results of the study showed that the onset and duration of the sensory and motor block with low dose and concentration was not significantly different from higher dose and concentration of the agent (15). Our both dosage and concentration was higher than this study and also the narcotic addition in our study was the other different point.

We have met clinical trials in the literature also that proved the similarity of block quality with axillary approach of both levobupivacaine and bupivacaine. Durra et al found no difference between levobupivacaine and bupivacaine in onset or duration of axillary plexus block on patients undergoing surgery of the forearm or hand (16). Liisanantti also performed a perivascular axillary brachial plexus block in hand and forearm surgery with 45 mL of 5 mg.mL\(^{-1}\) of either racemic bupivacaine-HCl, levobupivacaine-HCl, or
ropivacaine-HCl and pointed that time to onset and duration of block was similar in levobupivacaine and bupivacaine performed groups (17). In our study, time to sensory and motor block onset was significantly shorter in levobupivacaine administered groups (9.66 and 6.40 min) than bupivacaine administered group (13.40 and 9.20 min).

In a review of Foster pointed that levobupivacaine provided sensory block for up to 17 hours after brachial plexus block (4). As similar; in our study levobupivacaine provided approximately 17 and bupivacaine provided 18 hours duration of sensory block.

We have used morphine in conjunction to local anaesthetic solution in both groups. The dosage of morphine was maintained in both levobupivacaine and bupivacaine administered groups (2 mg, 0.05 mg/ml as concentration). Karakaya et al pointed out that the addition of 100 μg/mL fentanyl to 0.25% bupivacaine almost doubles the duration of analgesia following axillary brachial plexus block when compared with 0.25% bupivacaine alone (18). There are few clinical experiences that proved non-efficiency of narcotic addition to local anaesthetics in axillary block. Jamnig et al claimed that the addition of 100 microg. fentanyl to 50 mL mepivacaine does not improve the quality or duration of axillary plexus block regarding time to onset of block, duration of motor or sensory block, the VAS scores and the amount of analgesic needed (19).

Similarly Fanelli showed that addition of fentanyl 1 microg.mL⁻¹ to ropivacaine 7.5 mg.mL⁻¹ does not improve the nerve block characteristics of axillary brachial plexus anaesthesia for orthopaedic procedures (20). We thought that we should plan further trials investigating the difference of the block quality between with or without narcotic agents added to local anaesthetics.

We are aware of the fact that when the operation time was considered; the durations of the axillary blocks performed with both agents were unnecessarily long (17 h with levobupivacaine and 18 h with bupivacaine approximately). We thought this is associated with higher concentration and dosage and also morphine addition. This too longer sensory block duration gave a bit unwell sensation to patient and in our opinion should be shortened. But on the other hand long duration of first analgesic requirement time (levobupivacaine approximately 17 hours and bupivacaine approximately 18) provided comfortable postoperative period both for the patients and for the ward staff.

In conclusion; axillary brachial plexus blocks with 40 mL of 0.375 concentration of levobupivacaine and bupivacaine produced adequate anaesthesia without any significant difference in block duration and analgesic requirement time; but in our opinion levobupivacaine may be preferred for its rapid sensorial and motor onset time in situations surgeon’s impatience is considered, and also this can speed the circulations of the operation rooms up.

References

11. D’Ambrosio A, De Negri P, Damato A, Cavalluzzo A,


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